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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/553,978	04/20/2000	Paul L. Gourley	SD-6450/S-92.434	4921

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/553,978	GOURLEY, PAUL L.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants priority claim to application 09/489,274, filed January 21, 2000, which is a related to application 09/221,331, filed December 23, 1998. After review of the '274 application it is noted that there is no written description for a method of detecting cancer, or a method of a method of determining the phase of cells in the cell cycle, both methods dependent upon the discernment of G1 cells versus G2 cells within the laser biocavity. Accordingly, claims 1-5 drawn to the discernment of G1 cells versus G2 cells will be given the instant priority date of April 20, 2000.

Claims 1-6 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of claim 1 cannot be determined. Claim 1 recites "determining the shape of the G1 cells distribution, where an increased breath of the G1 distribution is an indication of increased cell growth rate". This phrase appears after the end of a sentence, and is appended to a method which recites determining the laser wavelength of the laser biocavity with only fluid in the microchannel; determining the wavelength shift of the biocavity when each cell passes through the microchannel; and determining the percentage of cells in G2 phase from the wavelength shift of the cells; wherein an increased percentages of G2 phase cells is an indication of cancer. It is unclear if the phrase that is attached to claim 1 is part of the claim, and further, it is unclear how the indication of increased growth rate relates to the method objective of detecting cancer. Further, it is unclear what the "increased breath of the G1 distribution" is

relative to. Claim 1 is also vague and indefinite because it is unclear how the first method step of determining the laser wavelength of the laser biocavity with only fluid in the microchannel is related to the second method step of determining the wavelength shift in the biocavity when each cell passes through, or determining the percentage of cells n the G2 phase.

Claim 2 is vague and indefinite in the recitation of "range where G2 phase cells are expected". without specific limitations for said range, the metes and bounds of the claim are unclear.

Claims 3 is vague and indefinite in the recitation of "range where G2 phase cells are expected", and "range where G1 phase cells are expected". without specific limitations for said range, the metes and bounds of the claim are unclear.

Claims 4 -6 are vague and indefinite in the recitation of "wavelength shift" without a recitation of the relative point from which said shift is measured.

Claim 4 is vague and indefinite as it is not clear how the determination of the laser wavelength in the fluid filled microchannel affects the determination of the wavelength shift of the biocavity when a cell passes through, or how the measurement of the fluid filled biocavity affects the determination of the phase of the cell.

Claim 5 is vague and indefinite in the recitation of "distinct values of wavelength shift" it is unclear what qualifies a numerical value to be a "distinct" value versus an indistinct value. claim5 is also vague and indefinite in the recitation of "increased number of cells in G2 phase" without an indication of what this increase is in comparison to. Claim 5 is also vague and indefinite in the recitation of "the number of data points" without an indication of the parameters of said data points.

It is unclear how the recitation of "determining from the wavelength shift the percentage of cells having a concentration greater than the concentration of a normal cell" in claim 6 relates to the method objective of determining cell concentration. Further, the recitation of "the percentage of cells" and "a normal cell" in claims 5 and 7 appears to have no antecedent basis within the claims which are drawn to the determination of cell concentration within a biocavity laser (according to the method objective) Said determination would yield only the number of cells per unit volume. What is meant by "percentage of cells having a concentration greater than

the concentration of a normal cell" in relation to determining the number of cells per unit volume cannot be construed from the claim language.

Claim 7 is vague and indefinite in the recitation of "predetermined amount". Without specific limitations for this predetermined amount, the metes and bounds of the claims cannot be determined.

Claims 1, 4 and 5 are vague and indefinite as it is unclear if the multiple recitations of wavelength shift refer to the same measured parameter.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the phase of cells in the cell cycle for a homogenous population of cells, does not reasonably provide enablement for a method of determining the phase of cells in the cell cycle for a heterogeneous population of cells, or a method of detecting cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

Claims 1-3 are drawn to method of detecting cancer using a laser biocavity having a semiconductor laser including a microchannel through which cells in fluid traverse, wherein said method comprises determining the laser wavelength shift of the biocavity when each cell passes through, followed by the determination of the percentage of cells in the G2 phase from the wavelength shift of the cells, wherein an increased percentage of G2 phase cells is indicative of cancer. Claim 4 is drawn to a method of determining the phase of cells in the cell cycle comprising determining the wavelength shift of the biocavity when a cell passes through the microchannel and determining the phase of the cell based on the wavelength shift. claim 5

embodies the method of claim 4 wherein the wavelength shift is determined for a plurality of cells, and the relative number of cells in the G1 and G2 phases are determined.

Thus the claims are broadly drawn to encompass the detection of cancer or the determination of the ratio of G1 to G2 in a sample taken from an in situ tumor, as well as the determination of the cell cycle in a homogenous population of cells, or tumor cells, such as cell in culture. The specification is not enabling for the detection of cancer from a sample taken from an in situ tumor or the determination of the phase of cells in the cell cycle from a sample taken from an in situ tumor. It is further noted that all types of cancers are included within the scope of the claims.

It is well known in the art that one of the major pitfalls for the analysis of the cell cycle in samples obtained in vivo is the frequent absence of pure cell populations, and that more often than not a mixture of different cell types exist at variable proportions which may present a different distribution along the distinct cell cycle phases, and thus it follows that the global analysis of the cell cycle in such samples does not provide direct information on the proliferation of each of the different subpopulations present in the sample (Orfao de Matos Correia e Vale, EP 798, 386, column 1, lines 36-45).

The art teaches that there are numerous lasing modes for a transparent object within a biocavity semi-conductor laser (Meissner et al, SPIE, 1995, Vol. 2399, pp. 561-570, figure 8). The art teaches that the nuclei of placental spindle cell tumor gave off a pattern of emitted light that was complex (Gourley, Nature Medicine, 1996, Vol. 2, pp. 942-944, page 943, figure 3, "spindle nuclei modes"), and that this pattern represents DNA/protein interactions within the cell (Gourley, Optics and Photonics News, 1997, Vol. 8, pp. 31-36, page 33, first column, lines 11-13 under the heading "Physics of the biological microcavity laser") . One of skill in the art would reasonably conclude that the laser spectrum of a range of different tumor cells derived from a sample taken from a patients would be complex and unpredictable due to the inherent heterogeneity of tumor cells with regard to ploidy and DNA/protein interactions. Thus, one of skill in the art would be subject to undue experimentation with regard to identifying which peak is G1 and which peak is G2. With regard to the acquisition of laser spectra from a population of cells, the art also teaches that when a population of cells are examined the pulse output will vary from cell to cell, and the spectrum will be a composite of distinct single cell spectra

comprising a peak near h=0 with other peaks at higher pulse heights, and that the number of these peaks will depend on the number of distinct cell types that dominate the distribution. (Gourley, Sandia National Laboratories Technical Report, 1997 (SAND97-1988), pp. 1-26, especially page 18, second full paragraph). Thus, one of skill in the art would expect a complex laser spectrum from every unique sample. Further, claim 5 requires that the determination of the relative number of G1 and G2 phase cells is by means of the "number of data points grouped about distinct values of wavelength shift" which for the reasons set forth under 12, second paragraph above, cannot be determined.

Claims 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 6 and 7 are rejected as having inadequate written description. Claims 6 and 7 are broadly drawn to methods relying on the identity a biocavity laser. thus the claims encompass a genus of biocavity lasers. the specification provides a written description of a laser cavity having the dimensions of a cell wherein one surface is a semi-conductor. The disclosure of the specific semi-conductor laser does not adequately describe all other possible materials which could be used in the laser surface. One of skill in the art would reasonably conclude that applicant was not in possession of a genus of biocavity lasers. It logically flows that if the specification lacks adequate written description for the structure of the laser on which the claimed methods depend, the claimed methods also lack adequate written description.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by the abstract of Uhal et al (American Respiratory Disease, 1991, vol. 143, no. 4, part 2, page A301) or Luther et al (Cytometry, 1996, Vol. 23, pp. 272-278).

The abstract of Uhal et al discloses the quantization of a fraction of G2/M phase cells in pneumonectomized rats versus normal rats.

Luther et al disclose the resolution of G2 cells versus G1 cells (page 276, figure 3) by means of laser scanning cytometry.

It is noted that claims 6 and 7 have been rejected under 112, second because the metes and bounds of said claims could not be determined. It appears that the disclosure of the abstract of Uhal et al or the disclosure of Luther et al fulfills the claim limitations. It is further noted that the biocavity laser relied upon for the method of claims 6 and 7 is not qualified as constituting a semiconductor as part of the components of the lasing cavity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (571) 272-0828. The examiner can normally be reached on Monday through Friday from 9 am to 6:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (571) 272-0871. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at 703-308-4357.

Karen A. Canella, Ph.D.
Primary Examiner, Group 1642
01/28/04